



PH-652 949-45

PATENT
Customer No. 22,852

MICROORGANISM DEPOSIT DECLARATION UNDER 37 C.F.R. § 1.808(a)

I do hereby declare and say that:

1. Chugai Seiyaku Kabushiki Kaisha is the assignee of the above-identified patent application.

2. On information and belief, the hybridoma clone which produces the #23-57-137-1 antibody was deposited with the National Institute of Bioscience and Human-Technology, Agency of Industrial Science and Technology on August 15, 1996 under Accession Number FERM BP-5631 to assure availability of the cell culture to the public.

3. On information and belief, the National Institute of Bioscience and Human-Technology, Agency of Industrial Science and Technology, Japan (1-3, Higashi 1-chome, Tsukuba-shi, Ibaraki-ken 305, Japan) has acquired the status of International Depository Authority within the meaning of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure.

4. Said culture has been deposited under conditions which ensure that access to the culture will be available during the pendency of this patent application to one determined by the Commissioner of Patents and Trademarks to be entitled thereto under 37 C.F.R. § 1.14 and 35 U.S.C. § 1.22.

5. No later than issuance of a patent on this application, Chugai Seiyaku Kabushiki Kaisha will irrevocably remove any restrictions as to public availability of

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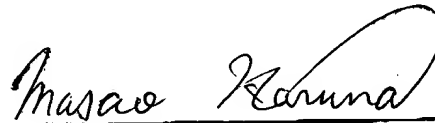
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this culture deposit except as permitted by 37 C.F.R. § 1.808(b), and will replace the culture deposit should it become nonviable, during the period that extends thirty years from the date of the deposit, or the period of the enforceable life of the patent, or the period of five years after the last public request for the deposit, whichever period is longest.

6. I further declare that all statements made herein of my own knowledge are true; that all statements made on information and belief are believed to be true; that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code; and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

July 31, 2002

Date



Name: Masao Haruna

Title: Director, Intellectual Property
Department of
CHUGAI SEIYAKU KABUSHIKI KAISHA

Serial No.: 09/269,332
Filed: March 25, 1999

**Title: ANTIBODIES AGAINST HUMAN PARATHYROID HORMONE
 RELATED PROTEIN**

By:

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ANTIBODIES AGAINST
HUMAN PARATHYROID HORMONE RELATED PROTEIN

TECHNICAL FIELD

The present invention relates to a human/mouse chimeric antibody comprising a variable region (V region) of a mouse monoclonal antibody against a parathyroid hormone related protein and a constant region (C region) of a human antibody, a humanized antibody in which complementarity determining regions of the light chain (L chain) and heavy chain (H chain) V regions of a mouse monoclonal antibody against a parathyroid hormone related protein (PTHrP) are grafted to a human antibody, the L and H chains of said antibody, as well as a polypeptide comprising the V region constituting the L or H chain of said antibody.

The present invention also relates to a DNA comprising a base sequence coding for the above mentioned antibody, particularly its V region, and a DNA coding for an L or H chain comprising the V region. Further, the present invention relates to a recombinant vector comprising said DNA and a host transformed with said vector.

Furthermore, the present invention relates to processes for preparing the chimeric and humanized antibodies against a PTHrP. Still further, the present invention relates to a pharmaceutical composition, and hypercalcemia-suppressing or hypophosphatemia-improving agent comprising the antibody against a PTHrP as an effective ingredient.

BACKGROUND OF THE INVENTION

Hypercalcemia associated with malignant tumor is a serious

ABSTRACT

The invention provides a therapeutic agent for hypercalcemic crisis comprising, as an active ingredient, a substance capable of inhibiting the binding between a parathyroid hormone related protein (PTHrP) and a receptor thereof.

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